

## REMARKS

## 1. Status of the Claims and Formal Matters

## a. Amendments

Claims 1, 8, 11-12, 14, 23 and 26 are pending in this application. Claims 2-7, 9-10, 13, 15-22 and 24-25 were previously cancelled. Claims 1 and 8 are amended. Upon entry of these amendments, claims 1, 8, 11-12, 14, 23 and 26 are pending and under active consideration. Applicants respectfully request entry of the supplemental amendments and remarks made herein into the file history of the present application.

Claim 1 is amended to recite that the nucleic acid consists of 77 up to 120 nucleotides, support for which may be found throughout the application including SEQ ID NO: 14. Claim 1 is also amended to recite that the nucleic acid comprises the sequence of SEQ ID NO: 14, support for which may be found in previous claim 1.

Claim 8 is amended to recite that the vector comprises an HIV nucleic acid, support for which may be found throughout the application as originally filed. Claim 8 is also amended to recite the HIV nucleic acid consists of the nucleic acid of claim 1 or claim 26, support for which may be found in previous claim 8.

## b. Interview Summary

The undersigned would like to thank Examiner Brusca and Examiner DeJong for the courtesy of the telephone interview of August 9, 2006 during which the cited art, claim scope, and possible amendments were discussed. It was agreed that claim 1 would be amended in the manner herein in order to address any remaining concerns under 35 U.S.C. § 112, second paragraph. Based on this agreement, Applicant makes a similar amendment herein to claim 8.

In addition, the deficiencies of Fire et al., *Nature* (1998) and similar references either or alone or in combination with other references were discussed. Although a rejection based on Fire et al. (or similar references) has not been made on the record, it was agreed by Applicant to address the failure of Fire et al. (and similar references) to teach or suggest the claimed nucleic acids in order to expedite prosecution of the instant application.

## 2. Deficiencies of Fire et al. (and Similar References)

Applicant respectfully submits that Fire et al. (and similar references) either alone or in combination with any other references fail to teach or suggest the instant claims. During the

interview, the Examiner characterized Fire et al. as teaching the design of double-stranded nucleic acids derived from a target gene for use in RNAi to reduce expression of the protein encoded by the target gene. The Examiner is considering that Fire et al. (and similar references) may teach of suggest the claimed nucleic acids because one of ordinary skill in the art would allegedly be motivated to use coding sequences (e.g., claims 1 and 26) together with complementary sequences (e.g., claim 23) derived from the HIV *gag* gene to inhibit expression of the protein encoded by the *gag* gene.

Applicant respectfully disagrees. In addition to other bases, Applicant respectfully submits that the instant claims are not taught or suggested by Fire et al. (and similar references) in combination with any other references due to the presence of a property unexpectedly not possessed by the prior art. *See See MPEP 716.02(a); In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (rejection of claims to compound structurally similar to the prior art compound was reversed because claimed compound unexpectedly possessed anti-inflammatory properties not possessed by the prior art compound).

As described in the application as filed, SEQ ID NO: 14 is a single-stranded nucleic acid that forms a hairpin with a partially double-stranded stem. As indicated in the Declaration of Dr. Eti Meirie (the “Meirie Declaration”) submitted herewith, SEQ ID NO: 14 has been validated to represent a miRNA precursor that is processed to yield a miRNA. *See* paragraphs 3-7.

It is important to note that the nucleic acids described by Fire et al. are not hairpins. Moreover, even if hairpins were produced by joining the pairs of complementary nucleic acids described by Fire et al, the stems of the resulting hairpins would be completely double-stranded except for the loop region of the hairpin. Applicant respectfully submits that the ability of a single-stranded molecule, such as a nucleic acid comprising SEQ ID NO: 14, to form a hairpin with only a partially double-stranded stem and be processed by Dicer to yield a miRNA is a property not taught or suggested in the prior art.

Applicant respectfully submits that the unexpected property of the claimed nucleic acids is also not a latent property of any prior art sequence derived from the HIV *gag* gene. As indicated at paragraphs 8-10 of the Meirie Declaration, three additional potential hairpins were identified within the *gag* gene using bioinformatic techniques; however, each potential hairpin received a palgrade score of zero. A palgrade score of zero means that each of these potential hairpins did not pass the minimal stringency criteria of approximately 98% of all known miRNA

precursor hairpins. *See* Bentwich et al. (2005). Therefore, the only single-stranded nucleic acids derived from the HIV *gag* gene that are likely to form a hairpin and be a substrate for Dicer are those nucleic acids that comprise SEQ ID NO: 14. *See* paragraph 10 of the Meirie Declaration.

Applicant also respectfully submits that the scope of the claimed nucleic acids are commensurate with the unexpected properties described herein. The “contributing cause” of the unexpected property is the stem and loop formed by SEQ ID NO: 14. As indicated at paragraph 10 of the Meirie Declaration, the SEQ ID NO: 14 precursor may have extensions at the 5’ and/or 3’ ends. This is consistent with the application, as filed, and Bentwich (2005) which indicate the importance of the stem and loop for recognition by Dicer and the possibility of varying hairpin sizes. As a result, the unexpected results relate not only to a nucleic acid consisting of SEQ ID NO: 14 (e.g., claim 26) but also to a nucleic acid of up to 120 nucleotides that comprises SEQ ID NO: 14 (e.g., claim 21).

In view of the above comments, Applicant respectfully request that Fire et al. (and similar references) in combination with any other references do not teach or suggest the instant claims.

### 3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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